REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the foregoing amendment and following remarks are respectfully requested. Claims 1, 2, 4-7 and 9 are currently pending in this application and remain at issue. This response is timely filed as it is accompanied by a petition for an extension of time to file in the first month (extended) and requisite fee. The applicants request entry of the foregoing amendment, as it will either place the application for allowance or place the application in better form for appeal.

In paragraph 2 of the official action, the examiner objected to the phrase "from the group consisting of 6.1...(a)...(b)..." in claim 6. The examiner suggested replacing the term "6.1" with "(a)." As suggested by the examiner, the applicants have amended claim 6 to reflect alphabetical organization of claim 6.

In paragraph 3 of the official action, the examiner objected to the recitation "other genes of the biosynthetic pathway of the desired L-amino acid of *E. coli*" in claim 2. The examiner suggested replacing this allegedly unclear phrase with "other *E. coli* genes of the biosynthetic pathway of the desired L-amino acid." Solely to expedite prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 2 and 5 without prejudice.

In paragraph 4 of the official action, the examiner objected to the recitation "process according to claims." The applicants have canceled claim 9 without prejudice, thus rendering the objection to this claim moot.

New claim 28 is directed to the process of claim 1, wherein constituents of the fermentation broth and the biomass in its entirety or portions thereof being isolated as a solid product together with said L-amino acids. Support for new claim 28 can be found throughout the specification, for example, original claim 1(c).

New claim 29 is directed to the process according to claim 1, wherein L-threonine is produced by fermenting the E. coli strain MG442ΔpckA deposited under DSM13761. Support for new claim 29 can be found throughout the specification, for example, on page 14, lines 15-20.

New claim 30 is directed to the process according to claim 1, wherein L-threonine is produced by fermenting E. coli strain B-3996kurΔtdhΔpckA/pVIC40 deposited under DSM14150. Support for new claim 30 can be found throughout the specification, for example, on page 14, lines 21-26.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications. The applicants request entry of the foregoing amendment in that the amendments overcome the present rejection or in the alternative, place the application in better form for allowance.

Patentability Remarks

Rejection Under 35 U.S.C. §112, Second Paragraph

In paragraphs 5-8, the examiner variously rejected claims 4 and 9 under 35 U.S.C. §112, second paragraph, for indefiniteness. Specifically, the examiner alleged it was unclear how the term "wherein the expression of the *pck*A gene is attenuated" in claim 4 further limited claim 1. Furthermore, the examiner asserted claim 9 as presented was a duplicate of claim 1.

Solely to expedite prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 4 and 9. Accordingly, the rejection of claims 4 and 9 under 35 U.S.C. §112, second paragraph, is moot.

Rejections Under 35 U.S.C. §112, First Paragraph

Written Description

In paragraphs 10-12 of the official action, the examiner rejected claims 1, 2, 4-7, and 9 under 35 U.S.C. §112, first paragraph, for allegedly lacking written descriptive support. Specifically, the examiner alleged that while an inactivating deletion has been taught with regard to the *pck*A gene, the specification fails to disclose which mutations in the *E. coli pck*A gene can be made to encode a gene product with low activity, *i.e.*, one with less activity than the wild type counterpart. In response, the applicants submit that these rejections have been rendered moot by amendment of the relevant claims.

Amended claim 1 is directed to a fermentation process for the preparation of a desired L-amino acid selected from the group consisting of L-threonine, L-isoleucine, L-valine, and L-lysine, wherein the following steps are carried out (a) fermentation of an *E.coli* strain in a fermentation broth for producing the desired L-amino acid, wherein the endogenous gene encoding phosphoenolpyruvate (PEP) carboxykinase (*pck*A gene) of *E.coli* is simply *inactivated* by one or more methods of mutagenesis selected from the group consisting of deletion, insertional mutagenesis due to homologous recombination, and transition or traversion mutagenesis with incorporation of a non-sense mutation in the *pck*A gene, (b) concentration of the fermentation broth to eliminate water and increase the concentration of said L-amino acids in the broth and *E.coli*, and (c) isolation of the L-amino acid, constituents of the fermentation broth and the biomass. Support for amended claim 1 can be found throughout the specification, for example, on page 7, lines 3-21.

The claimed fermentation process of claim 1 is now directed an *E. coli* strain with an inactive *pck*A gene, which has been acknowledged by the examiner as sufficiently described in the specification. As discussed above, claims 2, 4, 5, and 9 have been canceled without prejudice. Claims 6 and 7 depend from claim 1 and thus also encompass the requirement that the *pck*A gene of *E. coli* be deactivated by deletion. In view of the foregoing amendment and remarks, the applicants respectfully submit that the rejection of claims 1, 2, 4-7, and 9 under 35 U.S.C. §112, first paragraph, for lack of written descriptive support, has been overcome and should be withdrawn.

Enablement

In paragraphs 13-15 of the official action, the examiner rejected claims 1, 2, 4-7, and 9 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the examiner alleged that while the specification is enabling for a fermentation process (1) for the preparation of L-threonine, L-lysine, L-isoleucine, or L-valine using an *E. coli* cell modified such that the *E. coli pck*A gene contain inactivation deletion, (2) the process of (1) wherein the copy number of the following *E. coli* genes is increased or wherein said *E. coli* genes are placed under the control of a strong promoter, and (3) the process of (1) wherein the following *E. coli* genes contain an inactivating deletion, the specification does not teach a fermentation process for the preparation of L-threonine, L-lysine, L-isoleucine or L-valine use an *E. coli* cell modified in any way such that the (a) *E. coli pck*A gene is less active than its wild type counterpart, (b) the process of (a) wherein any *E. coli* gene associated with the

biosynthetic pathway of L-threonine, L-lysine, L-isoleucine, or L-valine is modified in any way to produce a protein with higher activity than the wild type counterpart, or wherein the *pck*A gene is modified such that the regulatory and/or catalytic properties of the *pck*A gene are reduced.

With regard to amended claim 1, the applicants submit the claimed fermentation process inactivates the *E. coli pck*A gene by one or more methods of mutagenesis selected from the group consisting of deletion, insertional mutagenesis due to homologous recombination, and transition or traversion mutagenesis with incorporation of a non-sense mutation in the *pck*A gene. Support for these particular methods of inactivating the *pck*A gene of *E. coli* are taught both in the examples and on page 7, lines 4-21 of the specification. One of skill in the art would easily and without undue experimentation be able to use the teachings of the referred textbooks on page 7 of the specification and perform the particular inactivating mutational procedures to inactivate the *pck*A gene of *E. coli*. Assays measuring for the *E. coli pck*A gene encoded activity were also well known in the art at the time of filing (see Appendix A, for example, page 1621 of Hou *et al., J. of Bact.* 177:1620-1623 [1995]); see Appendix B for Form PTO-1449. The mutation of the *pck*A gene is well within the level of ordinary skill in the art and as such there would be no undue experimentation to practice the claimed invention. In other words, one simply produces a mutation by well known methods and tests for gene product activity using well known assays tested (see Appendix A). Accordingly, amended claim 1 is fully enabled.

In view of the foregoing amendments, the applicants respectfully submit claims 1, 6, and 7 are fully enabled as acknowledged by the examiner. Accordingly, the applicants submit that the rejection of claims 1, 2, and 5-7 under 35 U.S.C. §112, first paragraph, has been overcome and should be withdrawn.

Rejection Under Nonstatutory Double Patenting

In paragraphs 30-33 of the official action, the examiner rejected claims 1, 4, and 5 under the judicially created doctrine of obviousness-type double patent as being unpatentable over claims 9 and 10 of co-pending application no. 10/076416, claims 12-14 of co-pending application no. 10/114043, claims 12-14 of co-pending application no. 10/114048, and claims 12-14 of co-pending application no. 10/114073. Specifically, the examiner alleged each of the conflicting claims (*i.e.*, claims 1, 4, and 5 vs. for example claims 9 and 10 of co-pending application no. 10/076416) are directed to a fermentation process for the production of an L-

amino acid which uses an Enterobacteriaceae modified such that is contains a PEP carboxykinase gene wherein the expression of said gene has been reduced or eliminated and wherein said microorganism further comprises a modification (attenuated *dgs*A, *ace*A, *pox*B or *fru*R gene) such that the metabolic pathways will no longer reduce the formation of the desired L-amino acid. In view of the foregoing amendments and remarks, the applicants traverse this rejection.

As discussed above, claim 4 has been canceled without prejudice. The applicants submit the rejection of claims 1 and 5 is no longer applicable in view of the foregoing amendments. Specifically, each of these claims are directed to a fermentation process for the preparation of L-threonine, L-isoleucine, L-valine or L-lysine by fermenting an *E.coli* strain with an **inactivated *pck*A gene**. Claims 12-14 of co-pending application no. 10/114043, claim 9 and 10 of co-pending application no. 10/076416, claims 12-14 of co-pending application no. 10/114048, and claims 12-14 of co-pending application no. 10/114073 are each directed to a fermentation process for the production of L-amino acids which uses an Enterobacteriaceae modified such that it contains either a modified *dgs*A, *pox*B, *ace*A, or *fru*R gene in combination with an attenuated or mutated *pck*A gene. Claims 1, 4, and 5 do not recite such a combination with the inactivated *pck*A gene. Accordingly, claims 1 and 5 are patentably distinct and cannot possibly be either anticipated or considered obvious in view of the disclosures of U.S. Patent Appl. Nos. 10/076416, 10/114043, 10/114048, and 10/114073.

In order to expedite prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, claim 4 has been canceled without prejudice thereby obviating the provisional rejection of this claim. In view of the foregoing amendments and remarks, the applicants respectfully submit that the rejection of claims 1 and 4, and 5 under the judicially created doctrine of obviousness-type double patenting, has been overcome and should be withdrawn.

CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

All objections and rejections having been addressed, it is respectfully submitted that the present application is in a condition for allowance and a Notice to that effect is earnestly solicited.

Respectfully submitted,
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